Bulletin of the World Health Organization, 62 (3): 357-366 (1984)

Indications and contraindications for vaccines used in the Expanded Programme on Immunization*

A. M. GALAZKA,[1] B. A. LAUER,[2] R. H. HENDERSON,[3] & J. KEJA[1]

The aim of the Expanded Programme on Immunization is to reduce morbidity and mortality from six diseases that can be prevented by immunization. In many countries the immunization coverage is still less than optimal; one of the reasons for this is the fact that frequently health workers are faced with long lists of contraindications to immunization.

The present review discusses the risks of adverse reactions after immunization and compares these risks with the complication rates following natural disease. It is concluded that the decision to withhold the benefits of immunization from an eligible child should not be taken lightly, particularly in areas where access to immunization services is limited and the incidence of the vaccine-preventable diseases is still high.

Malnutrition should be a prime indication for immunization. Low-grade fever, mild respiratory infection, or diarrhoea should not be considered a contraindication to immunization. Measles immunization of children who have to be admitted to hospital has been shown to reduce the overall mortality rates in paediatric wards. It is recommended that all countries should formulate their own national policy, carefully considering the risks of disease as well as the benefits and potential risks of immunization.

Immunization is one of the most powerful and cost-effective weapons of modern medicine. Immunization services, however, remain tragically underutilized in the world today. In developing countries, 0.5% of all newborns can be expected to become crippled from poliomyelitis; 1% can be expected to die from neonatal tetanus, 2% from pertussis, and 3% from measles. In all, some 5 million children die from these diseases each year: 10 children with each passing minute. These diseases are preventable with currently available vaccines if children can be immunized early enough in childhood.

The decision to withhold the benefits of immunization from an eligible child, whatever the reason, should not be taken lightly. Unfortunately, health workers in many countries are faced with long lists of contraindications which, when followed scrupulously, result in many children remaining unimmunized. The problem resulting from deferment of immunization is greatest where access to health services is limited and the morbidity and mortality from vaccine-preventable diseases are high. Immunization is frequently postponed if children are ill, malnourished, or about to be hospitalized. Yet, these are the very children who are most in need of immunization services. They are the ones most likely to die, should they acquire a vaccine-preventable disease.

The present review describes the benefits and risks of routine immunization of children with BCG, DPT, measles and poliomyelitis vaccines, and suggests circumstances where immunization may be in the child's best interests.

* From the Expanded Programme on Immunization (EPI), World Health Organization, 1211 Geneva 27, Switzerland. Requests for reprints should be addressed to Dr R. H. Henderson. A French translation of this article will appear in a later issue of the *Bulletin*.

[1] Medical Officer, EPI, World Health Organization, Geneva.

[2] Consultant (Present address: Associate Professor of Pediatrics and Medicine, University of Colorado, Denver, CO, USA).

[3] Director, EPI, World Health Organization, Geneva.

ADVERSE REACTIONS TO IMMUNIZATION

Despite the high safety of the vaccines used in the Expanded Programme on Immunization (EPI), complications do occur. Although their rates are difficult to estimate precisely, it is known that they are far less frequent than the complications caused by the diseases themselves (see Tables 1-3). Some conditions, particularly fever and neurological syndromes, also occur spontaneously among unimmunized children. Against this background of disease, it is sometimes difficult to determine if a recent immunization is causally or merely coincidentally related to a child's illness. Convulsions, for example, may follow DPT or measles immunization, but the background rate is high; at ages 3-15 months, the monthly incidence rate of convulsions ranges from 0.8 to 1.4 per 1000 children (*20*, *65*).

BCG immunization

The most serious complications of BCG immunization are disseminated infection with the BCG bacillus and BCG osteitis (Table 1). Both of these complications are rare. The former is usually associated with severe abnormalities of cellular immunity (*28*, *63*), whereas the latter has been reported mainly among infants immunized in the neonatal period in the Scandinavian countries (*12*, *19*, *66*). The most common complication, suppurative lymphadenitis, has been reported in 0.1% to 4% of immunized children under two years of age. The risk of adverse reactions is related to the BCG strain used by different manufacturers, the dose, the age of the child, the method of immunization, and the skill of the vaccinator.

DPT immunization

The most severe complications following DPT immunization are neurological and are thought to be due primarily to the pertussis component of the vaccine. In a recent large study in the United Kingdom, the National Childhood Encephalopathy Study, the immunization histories of children aged two months to three years old and hospitalized with serious acute neurological illnesses (encephalitis/encephalopathy, prolonged convulsions, infantile spasms, and Reye's syndrome) were reviewed and compared with a control group (*21*, *56*). It was estimated that a severe neurological illness attributable to DPT occurred once in 110 000 DPT immunization doses and that lasting neurological damage occurred once in 310 000 immunization doses. In the continuation of the study, where altogether 1182 cases of neurological illness were analysed, the estimated risk of illness attributable to DPT was 1:170 000 doses administered, while that for permanent sequelae was 1:470 000 doses.[a] No evidence was found that pertussis vaccine is a direct causal factor for infantile spasms (*9*, *29*), although it was suggested that the vaccine may trigger the onset of infantile spasms in those children who were destined to develop the disease (*9*).

Table 1. Estimated rates of adverse reactions following BCG immunization

Adverse reaction	Estimated adverse reaction rate/ 100 000 vaccinees	References
Disseminated BCG infection	< 0.1	*46, 48, 66*
Osteitis/ osteomyelitis	< 0.1-30	*12, 19, 48, 66*
Suppurative adenitis (children below 2 years)	100-4300 (0.1-4.3%)	*30, 33, 45, 47, 49, 62, 63, 66*

[a] MILLER, D. L. *Current knowledge on pertussis vaccine: efficacy and safety.* XVII International Congress of Pediatrics. Pre-congress Workshop on Immunization, Manila, 6-7 November 1983 (WHO unpublished document WHO/IPA/WP/83.4).

The hazards of DPT immunization must, however, be balanced against the risks of remaining unimmunized. Convulsions, for example, occur more often during whooping cough than following DPT immunization and pertussis may be a cause of encephalopathy or death (Table 2).

Fever and mild local reactions following DPT immunization are common. It is estimated that 2–6% of vaccinees develop fever of 39 °C or higher and that 5–10% experience swelling and induration or pain lasting more than 48 hours at the site of injection. In studies in the United States and Australia, about 50% of children had local reactions (*7*, *8*, *17*, *27*).

Measles immunization

Severe reactions following measles immunization are rare (Table 3). In the United States, neurological disorders, including encephalitis and encephalopathy, have been reported once for approximately every million vaccine doses administered (*2*). However, the

Table 2. Estimated rates of adverse reactions following DPT immunization compared to complications of natural whooping cough

Adverse reaction	Whooping cough complication rates/ 100 000 cases	DPT vaccine adverse reaction rates/ 100 000 immunizations	References
Permanent brain damage	600–2000 (0.6–2.0%)	0.2–0.6	*10*, *21*, *23*, *36*, *61* and footnote *a* (p. 358)
Death	100–4000 (0.1–4.0%)	0.2	*14*, *22*, *24*, *36*, *43*, *61*, *64*, *68*
Encephalopathy/encephalitis[a]	90–4000 (0.09–4.0%)	0.1–3.0	*3*, *14*, *21*, *26*, *35–37*, *43*, *61*, *64*, *71* and footnote *a* (p. 358)
Convulsions	600–8000 (0.6–8.0%)	0.3–90	*3*, *14*, *17*, *26*, *27*, *35–38*, *43*, *64*, *68*, *71*
Shock	–	0.5–30	*3*, *37*

[a] Including seizures, focal neurological signs, coma, and Reye's syndrome.

Table 3. Estimated rates of serious adverse reactions following measles immunization compared to complications of natural measles infection and background rate of illness

Adverse reaction	Measles complication rates/100 000 cases	Measles vaccine adverse reaction rates/100 000 vaccinees	Background illness rate/100 000 persons	References
Encephalitis/ encephalopathy	50–400 (0.05–0.4%)	0.1	0.1–0.3	*2*, *44*, *55*
Subacute sclerosing panencephalitis	0.5–2.0	0.05–0.1	–	*35*, *36*, *57*
Pneumonia	3800–7300 (3.8–7.3%)	–	–	*36*, *55*
Convulsions	500–1000 (0.5–1.0%)	0.02–190	30	*35*, *36*, *38*, *44*, *53–55*, *59*
Death	10–10 000 (0.01–10%)	0.02–0.3	–	*2*, *4*, *22*, *36*, *55*

reported incidence rate of encephalitis or encephalopathy following measles immunization is lower than the observed incidence rate of encephalitis of unknown etiology, which is 2 per 1 million children per 28-day period (*44*). This suggests that some of the reported severe neurological disorders may not be caused by measles immunization but related only in time. In the United Kingdom, however, the National Childhood Encephalopathy Study found a statistically significant association between the onset of acute neurological illness and measles immunization given 7–14 days before the onset of illness in cases compared with controls. The relative risk for this period was estimated to be 2.5 times the background rate (*21*).

About 5–15% of measles vaccinees develop a temperature of 39.4 °C or higher, beginning on the sixth day and usually lasting one or two days. Transient rash may occur in about 5% of vaccinees (*2*).

Measles immunization, by preventing natural measles, reduces the risk of developing subacute sclerosing panencephalitis (SSPE) (*2*).

Poliomyelitis immunization

Paralytic polio is the only serious adverse reaction associated with oral poliomyelitis vaccine. The risk is increased in immunodeficient children. In a 10-year WHO Collaborative Study, the risk of vaccine-associated paralysis was estimated to be about one case per million vaccinees and the risk of a close contact of a vaccinee developing paralytic polio was one case per approximately 5 million doses of vaccine distributed (*69*). In the United States the reported risk of paralysis in vaccinees or their close contacts was one case per 3.2 million doses distributed (*1*).

Serious adverse reactions to inactivated poliomyelitis vaccines currently in use have not been reported.

IMMUNIZATION OF ILL OR MALNOURISHED CHILDREN

Health personnel are understandably cautious in offering immunization to any child who is not healthy. But, as already discussed, such children may be particularly benefited by immunization. In most cases, it is safe and effective.

The most ample literature on this subject concerns measles immunization. Several studies have investigated measles immunization of malnourished or ill children. McMurray et al. (*52*) studied serum antibody responses and reaction rates to measles vaccine in normal and moderately malnourished 10-month-old Colombian children who were followed up for more than a year. Malnourished children had high measles antibody responses and had no more adverse reactions than well-nourished children. The authors concluded that measles vaccine is both safe and effective in moderately malnourished children.

Ifekwunigwe et al. (*41*) studied serum antibody responses and adverse reactions following measles immunization of malnourished Nigerian children aged 5 months to 9 years old. Malnutrition did not impair the children's serological responses; of 111 children who were seronegative before immunization, 94% seroconverted. There were no major adverse reactions to immunization during the 8-week follow-up period. The authors concluded that malnutrition should be a prime *indication* for measles immunization rather than a contraindication because antibody responses are normal and because natural measles is often severe in malnourished children.

In most other studies, nutritional status appeared to have no significant effect on measles seroconversion rates when measles vaccine was administered alone (*11*, *15*, *18*, *50*) or

Table 4. Measles immunization of ill children in three African studies

Country (reference)	Children		Type of illness[a]	Adverse reactions[a]	Effect of immunization
	No.	Age (months)			
1. S. Africa (*67*)	214	6–60	All patients admitted consecutively to hospital.	Temperature ⩾ 38.9 °C (12%) Koplik's spots and rash (8%)	Reduced nosocomial measles, compared with control wards
2. Zimbabwe (Rhodesia) (*32*)	98	6–32	Hospital patients with gastroenteritis (40%), broncho-pneumonia (30%), malnutrition (12%), other respiratory infection (6%), meningitis (3%), and other illness (9%).	Temperature ⩾ 38.9 °C (13%) Rash (4%)	Reduced nosocomial measles, compared with unimmunized control group
3. S. Africa (*39*)	654	7–36	Hospital patients with gastro-enteritis (35%), cardiac and renal diseases (35%), bronchopneumonia (17%), and kwashiorkor and marasmus (12%).		No nosocomial measles, compared with 9 cases and 3 deaths noted in the previous year. Overall mortality dropped by 49%

[a] Figures in parentheses are percentage frequencies.

simultaneously with DPT vaccine (*50*). In one investigation, however, children with severe kwashiorkor had impaired responses to measles immunization compared with well children (*60*).

The results of three studies of measles immunization of ill children in hospital are shown in Table 4 (*32*, *39*, *67*). The studies were conducted in paediatric wards during efforts to control hospital-acquired measles, which is a cause of high morbidity and mortality. Children with a wide range of acute and chronic illnesses were included; reasons for exclusion were a terminal illness, a history of measles, steroid therapy, or an immunological disorder. The authors concluded that measles immunization of ill or malnourished children did not appear to adversely affect the course of the children's illnesses and that the risk of measles cross-infection in paediatric wards practising measles immunization was diminished considerably.

In Ivory Coast a policy of immunizing sick children was introduced in 1981.[b] All children between 9 and 35 months of age who visited the health centres because of illness other than measles were screened; if unimmunized against measles, they were immunized. The introduction of the new policy resulted in a near doubling of the number of doses of measles vaccine administered from 26 000 to 45 000 doses in comparable 6-month periods.

Limited data are available concerning the use of the other EPI vaccines in malnourished or ill children. The use of DPT (*31*), BCG (*47*), and poliomyelitis (*13*) vaccines in moderately malnourished children appears to be safe.

Responses to diphtheria toxoid of severely ill or malnourished adults (*6*, *40*) or malnourished children (*31*, *70*) do not differ significantly from the responses of well nourished individuals.

Responses to tetanus toxoid of malnourished children also appear to be normal (*25*, *31*, *42*). Sick children with respiratory infection, gastroenteritis, and febrile illness (excluding

[b] COFFI EMMOU. Paper presented at the International Symposium on Measles Immunization, Washington DC, 16–19 March 1982 (unpublished).

malaria) appear to respond like healthy controls to tetanus toxoid (*34*). Malaria has been shown in some studies to inhibit the antibody response to tetanus toxoid (*25*, *34*, *51*). In two of these studies (*34*, *51*), however, only one or two doses of unadsorbed rather than adsorbed tetanus toxoid was given. In more recent studies (*58*),[c] malaria had no major effect on the serological response to adsorbed tetanus toxoid, measles or DPT vaccines. There is no evidence of increased rates of adverse reaction following immunization of children with malaria.

Serum neutralizing antibody titres following a single dose of trivalent oral poliomyelitis vaccine were found to be similar in malnourished and well-nourished children (*15*, *16*). However, in malnourished children secretory IgA antibody was detected significantly less often, its appearance was delayed, and the levels were significantly lower.

Considerable evidence suggests that injections, including immunizations, may provoke paralysis in the injected limb of children who are in the incubation period of polio infection. This is partly the reason why the authorities in some areas without poliomyelitis immunization programmes have recommended that DPT be withheld from febrile children. A small risk of injection-provoked paralysis may exist in polio endemic areas, but fever is neither a sensitive nor a specific sign of polio infection. It seems likely that withholding DPT immunization from febrile children would result in deaths from pertussis which would far outnumber the cases of injection-provoked poliomyelitis. Concern about injection-provoked poliomyelitis provides a strong argument in favour of polio immunization simultaneously with DPT at an early age, before the infants are at a high risk of exposure to wild poliovirus.

VARIATIONS IN NATIONAL POLICIES CONCERNING CONTRAINDICATIONS TO IMMUNIZATION

Countries vary in their policies concerning possible contraindications to immunization, some agreeing and sometimes differing. The policies are often based on theoretical concerns rather than facts; much needed data are frequently lacking. There is general agreement that immunization should be deferred in the presence of a severe febrile illness (*5*, *21*). The reasons are to avoid the risk of superimposing possible adverse effects from the vaccine on the underlying febrile disease, and to avoid a manifestation of the illness being attributed to the immunization.

There is also a consensus that vaccines requiring multiple doses such as DPT should not be repeated if a severe reaction occurred after a previous dose. Such reactions include collapse or shock-like state, persistent screaming episodes, temperature above 40.5 °C, convulsions, severe alterations in consciousness or other neurological symptoms, and anaphylactic reactions. In the case of DPT, subsequent immunization with diphtheria and tetanus toxoid is recommended. Local reactions at the site of injection or mild fever do not by themselves preclude the further use of DPT or other vaccines. Also, live vaccines should not be administered to persons with immune deficiency diseases or to persons whose immune response may be suppressed because of leukaemia, lymphoma, generalized malignancy, or therapy with corticosteroids, alkylating agents, antimetabolic agents or radiation.

There is disagreement about other issues. For simplicity a few examples have been selected from two English-speaking countries, the United Kingdom and the United States of America, both of which have well developed immunization services and both of which

BREMAN, J. G. ET AL. *Malaria and immunodepression: is there an effect on seroconversion following childhood immunization?* Paper presented at the Annual Meeting of the American Society of Tropical Medicine and Hygiene, November 1982.

have clear national recommendations concerning the indications for immunization. In the United Kingdom, the Department of Health and Social Security includes untreated tuberculosis as a contraindication to measles immunization, and recommends that children with a history of convulsions, epilepsy, and chronic heart or lung disease, or who are seriously underdeveloped, should be given measles vaccine only with the simultaneous administration of human immunoglobulin (*21*). The United States Public Health Service Advisory Committee on Immunization Practices (ACIP), on the other hand, finds no convincing evidence that measles immunization exacerbates tuberculosis and concludes that the benefit of measles immunization far outweighs the theoretical risk of exacerbation of tuberculosis (*2*). The ACIP recommends that measles vaccine should *never* be administered simultaneously with immunoglobulin and does not recognize any neurological contraindication to measles immunization.

In the United Kingdom, but not in the United States of America, gastrointestinal disturbances, including diarrhoea, are considered a contraindication to oral poliomyelitis immunization (*1*, *21*). In the United Kingdom, a family history of neurological disease and developmental defects are contraindications to DPT immunization (*21*). In the USA an evolving neurological disorder is considered a contraindication, but not a static neurological disorder such as cerebral palsy or a family history of neurological disease (*3*).

RECOMMENDATIONS OF THE EXPANDED PROGRAMME ON IMMUNIZATION

Lack of resources which include staff, supplies and equipment is the major constraint to the delivery of effective immunization services in developing countries. Incomplete implementation of immunization policies is the main problem in the industrial countries. Immunization policies that are needlessly restrictive can aggravate these problems.

It does not seem feasible or desirable to formulate a universal set of recommendations for immunization of children. Each country should formulate its own policies, preferably based on the advice of a broadly constituted advisory group. The recommended national policy should reflect a practical appraisal of the risks of the disease as well as the benefits and potential risks of immunization. Important considerations include the availability and accessibility of health care services, utilization patterns of these services, the ability to identify and follow-up children who are not immunized, the likelihood that children will return for subsequent immunization, and sociocultural acceptability of specific procedures and recommendations. The principal recommendations, which can serve as a general guide, include the following.

— Health workers should use every opportunity to immunize eligible children.

— BCG can safely and effectively be given in the newborn period, and DPT and oral polio vaccine at as early as six weeks of life (and, in certain situations, even earlier). In countries where measles poses a major burden before the first birthday, measles vaccine should ordinarily be given at the age of 9 months.

— No vaccine is totally without adverse reactions, but the risks of serious complications from vaccines used in the Expanded Programme on Immunization are much lower than the risks from the natural diseases.

— The decision to withhold immunization should be taken only after serious consideration of the potential consequences for the individual child and the community.

— It is particularly important to immunize children with malnutrition. Low grade fever, mild respiratory infections or diarrhoea, and other minor illnesses should not be considered as contraindications to immunization.

— Immunization of children who are so ill as to require hospitalization should be deferred for decision by the hospital authorities.

— The immunization status of hospitalized children should be evaluated, and they should receive appropriate immunization before discharge (in some cases they should be immunized on admission, because of the high risk of hospital-acquired measles).

— A second or third DPT injection should not be given to a child who has suffered a severe adverse reaction to the previous dose. The pertussis component should be omitted and diphtheria and tetanus immunization completed.

— Diarrhoea should not be considered a contraindication to oral polio vaccine but, to ensure full protection, doses given to children with diarrhoea should not be counted as part of the series and the child should be given another dose at the first available opportunity.

ACKNOWLEDGEMENTS

The authors would like to thank the members of the EPI Global Advisory Group, EPI Regional Advisers, paediatricians including members of the International Pediatric Association, epidemiologists, and all other persons who contributed their constructive and valuable comments, suggestions and proposals during the preparation of this paper.

REFERENCES

1. Recommendation of the Immunization Practices Advisory Committee: poliomyelitis prevention. *Morb. mortal. wkly rep.*, **31**: 22-34 (1982).
2. Recommendation of the Immunization Practices Advisory Committee: measles prevention. *Morb. mortal. wkly rep.*, **31**: 217-231 (1982).
3. Recommendation of the Immunization Practices Advisory Committee: diphtheria, tetanus and pertussis—guidelines for vaccine prophylaxis and other prevention measures. *Morb. mortal. wkly rep.*, **30**: 392-407 (1981).
4. BENENSON, A. S., ed., *Control of communicable diseases in man*, 13th edition, Washington DC, The American Public Health Association, 1980, pp. 211-215.
5. Recommendations of the Immunization Practices Advisory Committee: general recommendations on immunization. *Morb. mortal. wkly rep.*, **32**: 1-17 (1983).
6. BALCH, H. H. *J. immunol.*, **64**: 397-410 (1950).
7. BARAFF, L. J. & CHERRY, J. D. In: Manclark, C. R. & Hill, J. C., ed., *International Symposium on Pertussis*. Washington DC, U.S. Department of Health, Education and Welfare, 1979 (Publication No. (NIH)79-1830), pp. 291-296.
8. BARKIN, R. & PICHICHERO, M. E. *Pediatrics*, **63**: 256-260 (1979).
9. BELLMAN, M. H. ET AL. *Lancet*, **1**: 1031-1034 (1983).
10. BERG, J. M. *Arch. dis. child.*, **34**: 322-324 (1959).
11. BHATNAGAR, S. K. ET AL. *Indian pediatr.*, **18**: 625-629 (1981).
12. BÖTTIGER, M. ET AL. *Acta paediatr. Scand.*, **71**: 471-478 (1982).
13. BROWN, R. E. & KATZ, M. *East Afric. med. j.*, **42**: 221-232 (1965).
14. Pertussis surveillance, 1979-1981. *Morb. mortal. wkly rep.*, **31**: 333-336 (1982).
15. CHANDRA, R. K., *Brit. med. j.*, **2**: 583-585 (1975).
16. CHANDRA, R. K. *Brit. med. bull.*, **37**: 89-94 (1981).
17. CODY, C. L. ET AL. *Pediatrics*, **68**: 650-660 (1981).
18. COLLABORATIVE STUDY BY THE MINISTRIES OF HEALTH OF BRAZIL, CHILE, COSTA RICA AND ECUADOR, AND THE PAN AMERICAN HEALTH ORGANIZATION. Seroconversion rates and measles antibody titers induced by measles vaccine in Latin American children 6-12 months of age. *Bull. Pan Am. Hlth Org.*, **16**: 272-285 (1982).

19. DAHLSTROM, G. & SJOGREN, I. *J. biol. standard.*, **5**: 147-148 (1977).
20. DEPARTMENT OF HEALTH AND SOCIAL SECURITY. *Whooping cough vaccination. Review of the evidence of whooping cough vaccination by the Joint Committee on Vaccination and Immunization.* London, HMSO, 1977.
21. DEPARTMENT OF HEALTH AND SOCIAL SECURITY. *Whooping cough: reports from the Committee on Safety of Medicines and the Joint Committee on Vaccination and Immunization.* London, HMSO, 1981.
22. DITTMAN, S. *Atypische Verläufe nach Schutzimpfungen.* Leipzig, J. Ambrosius Barth Verlag, 1981.
23. Further contributions to the pertussis vaccine debate. *Lancet*, **1**: 1113-1114 (1981).
24. Immunization against whooping cough. *WHO Chronicle*, **29**: 365-367 (1975).
25. EDSALL, G. ET AL. In: *Proceedings of the Fourth International Conference on Tetanus, Dakar, 6-12 April 1975.* Lyon, Fondation Mérieux, 1975, vol. 2, pp. 683-685.
26. ERDOS, L. *Ann. immunol. Hung.*, **19**: 25-35 (1979).
27. FEERY, B. J. *Med. j. Austral.*, **2**: 511-515 (1982).
28. FISHER, A. ET AL. *Clin. immunol. immunopath.*, **17**: 296-306 (1980).
29. FUKUYAMA, Y. ET AL. *Neuropädiatre*, **8**: 224-237 (1977).
30. GHEORGHIU, M. ET AL. *Develop. biol. standard.*, **41**: 79-84 (1978).
31. GHOSH, S. ET AL. *Indian pediatr.*, **17**: 123-125 (1980).
32. GLYN-JONES, R. *Centr. Afr. j. med.*, **18**: 4-9 (1972).
33. GODDARD, N. & D'SOUZA, A. *CAREC surveillance rep.*, **9**: 1-5 (1983).
34. GREENWOOD, B. M. ET AL. *Lancet*, **1**: 169-172 (1972).
35. HALSEY, N. A. & STETLER, H. C. Adverse reactions associated with vaccines administered in Expanded Programme on Immunization projects. In: Halsey, N. A. & de Quadros, C. A., ed., *Recent advances in immunization. A bibliographic review.* Washington, Pan American Health Organization, 1983 (Scientific Publication No. 451), pp. 90-102.
36. HALSEY, N. A. Reactions to commonly used vaccines. In: Clark, D. W. & MacMahon, B., ed., *Preventive and Community Medicine*, Boston, Little, Brown & Co., 2nd ed., 1981, pp. 547-549.
37. HANNIK, C. A. & COHEN, H. In: Manclark, C. R. & Hill, J. C., ed., *International Symposium on Pertussis.* Washington DC, U.S. Department of Health, Education and Welfare, 1979. (Publication No. (NIH)79-1830), pp. 279-282.
38. HARKER, P. *Brit. med. j.*, **2**: 490-493 (1977).
39. HARRIS, M. F. *South Afric. med. j.*, **55**: 38 (1979).
40. HAVENS, W. P. ET AL. *Am. j. med. sci.*, **228**: 251-255 (1954).
41. IFEKWUNIGWE, A. E. ET AL. *Amer. j. clin. nutr.*, **33**: 621-624 (1980).
42. KIELMANN, A. A. ET AL. *Bull. Wld Hlth Org.*, **54**: 477-483 (1976).
43. KOPLAN, J. P. ET AL. *New Engl. j. med.*, **301**: 906-911 (1979).
44. LANDRIGAN, P. J. & WITTE, J. J. *J. Am. Med. Assoc.*, **223**: 1459-1462 (1973).
45. LEHMANN, H. G. ET AL. *Develop. biol. standard.*, **43**: 133-136 (1979).
46. LOTTE, A. ET AL. *Develop. biol. standard*, **43**: 111-119 (1979).
47. MANDE, R. *BCG vaccination.* London, Dawsons, 1968.
48. MANDE, R. *J. biol. standard.*, **5**: 155-158 (1977).
49. MANDE, R. ET AL. *Ann. pediatr.*, **23**: 219-225 (1976).
50. MARSHALL, R. ET AL. *J. trop. pediatr.*, **20**: 126-129 (1974).
51. MCGREGOR, I. A. & BARR, M. *Trans. Roy. Soc. Trop. Med. Hyg.*, **56**: 364-367 (1962).
52. MCMURRAY, D. N. ET AL. *Bull. Pan Am. Hlth Org.*, **13**: 52-57 (1979).
53. MEDICAL RESEARCH COUNCIL. *Brit. med. j.*, **1**: 441-446 (1966).
54. MILLER, C. *Practitioner*, **226**: 535-537 (1982).
55. MILLER, C. *Brit. med. j.*, **1**: 1253 (1978).
56. MILLER, D. L. ET AL. *Brit. med. j.*, **282**: 1595-1599 (1981).
57. MODLIN, J. ET AL. *Pediatrics*, **59**: 505-512 (1977).
58. MONJOUR, L. ET AL. *Bull. Wld Hlth Org.*, **60**: 589-596 (1982).
59. POLLOCK, T. M. *Rev. infect. dis.*, **5**: 574-576 (1983).
60. POWELL, G. M. *Ann. trop. paediatr.*, **2**: 143-145 (1982).
61. PSTRAGOWASKA, W. ET AL. *Pediatr. Pol. (Warsaw)*, **44**: 715-721 (1979).
62. REY, M. *Cah. méd.*, **5** (19): 1141-1146 (1980).

63. ROSENTHAL, S. R. *BCG vaccine: tuberculosis—cancer.* Littleton, Massachusetts, PSG Publishing Company, 1980.
64. ROYAL COLLEGE OF GENERAL PRACTITIONERS. *Brit. med. j.*, **282**: 23–26 (1981).
65. TUNSTALL PEDOE, H. & ROSE, G. In: *Whooping cough. Reports from the Committee on Safety of Medicines and Joint Committee on Vaccination and Immunization.* London, HMSO, 1981, pp. 50–54.
66. WAALER, H. & ROUILLON, A. *Bull. Int. Union Tuberc.*, **49**: 166–189 (1974).
67. WAGSTAFF, L. A. *South Afr. med. j.*, **43**: 664–669 (1969).
68. WALKER, E. ET AL. *J. infection*, **3**: 150–158 (1981).
69. WHO CONSULTATIVE GROUP. The relation between acute persisting spinal paralysis and poliomyelitis vaccine—results of a ten-year enquiry. *Bull. Wld Hlth Org.*, **60**: 231–242 (1982).
70. YAKACIKLI, S. ET AL. *Nutr. rep. intern.*, **9**: 427–431 (1974).
71. ZAMORA, D. A. ET AL. *Rev. Assoc. Med. Argent.*, **76**: 121–127 (1962).